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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,861	07/03/2002	Carlos Cordon-Cardo	55293-B-PCT-US/JPW/FHB	6709

7590 12/21/2005

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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,861	CORDON-CARDO ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *August 6, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *19,28 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *19,28 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendment filed August 6, 2005 and the Declaration filed August 6 2005 in response to the Office Action of February 3, 2005 is acknowledged and has been entered. Previously pending claims 1, 2, 4-6, 9-16, 18, 25-27, 29 have been cancelled, claim 19 has been amended. Claims 19, 28 and 30 are currently being examined.

2. Examiner appreciates Applicant's reference to the inadvertent error, wherein the invention of Group I, rather than the elected invention of Group II was examined. Group I is properly considered in this action and Examiner apologizes for any inconvenience.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The following rejections are being maintained:

Claim Rejections - 35 USC 103

5. Claim 19 remains rejected under 35 USC 103 for the reasons previously set forth in the paper mailed February 3, 2005, Section 11, pages 10-13.

Applicant argues that the cited references do not render the claimed invention obvious because the combined teaching would not have lead one of ordinary skill in the art to reasonably expect that an anti-Her-2/neu antibody could be used to treat androgen-independent prostate cancer. The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the rejected claim as currently constituted. In particular, claim 19 is drawn to treatment of prostate cancer and does not mention hormone state.

Applicant's arguments have not been found persuasive and the rejection is maintained.

6. Claims 19 and 28 remain rejected under 35 USC 103 for the reasons previously set forth in the paper mailed February 3, 2005, Section 112, pages 13-14.

Applicant argues that without experimentation, one of ordinary skill cannot reasonably predict that a successful anti-cancer outcome will occur using a particular combination of two drugs, even though each drug, when used individually has anti-cancer effects. Applicant states that in studies of patients with stage IV renal cell cancer, researchers found that attempts to combine known renal cancer fighting drugs, i.e. Proleukin and alfa interferon have been unsuccessful and points to Exhibit B, an overview of Stage IV Renal Cancer and states. Applicant further states that, apparently based on this evidence, each specific combination of two or more anti-cancer agents must be tested before one of skill in the art can know that such a combination will be effective against cancer, let alone more effective than either agent alone. The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the claims as currently constituted, Applicant is not claiming either an additive or synergistic effect. In addition, contrary to Applicant's arguments, the reference does not state that the combination of the two drugs was unsuccessful in treating cancer, rather the reference teaches that the combination of other drugs with Proleukin has not been associated with better results than treatment with Proleukin alone. The arguments have been considered but have not been found persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC 112

7. Claims 19, 28 and claim 30 are rejected under 35 USC 112, first paragraph because the specification, while enabling for a method of treating prostate cancer in a subject in need of such treatment wherein said prostate cancer overexpresses HER-2/neu comprising administering to the subject therapeutically effective amounts of humanized monoclonal antibody that is selective for the extracellular domain of the Her-2/neu protein does not reasonably provide enablement for said method wherein said humanized monoclonal antibody is specific for the extracellular domain of the Her-2/neu protein. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected to practice the invention commensurate in scope with these claims.

The claims are drawn to a method of treating prostate cancer in a subject in need of such treatment wherein said prostate cancer overexpresses HER-2/neu comprising administering to the subject therapeutically effective amounts of humanized monoclonal antibody that is specific for the extracellular domain of the Her-2/neu protein. This means that the claims are drawn to said method with any antibody that binds to the extracellular domain or HER-2/neu regardless of whether it cross reacts with other antigens including EGF receptor.

The specification teaches the immunohistochemically identified membrane overexpression of HER-2/neu in primary prostate cancer samples, see pages 87-96, and further teaches the treatment, in pre-clinical models, of cell-line derived androgen-dependent and androgen-independent sublines of CWR22 with the known, effective HER-2/neu antibody, HERCEPTIN (para bridging pages 103-104).

One cannot extrapolate the teaching of the specification to the scope of the claims because it is well known in the art, as previously set forth in the paper mailed February 3, 2005, pages 5-6, that HER-2/neu is a member of the EGFR family and shares homology with other members of the family. Given the shared homology, it would be expected that antibodies that were not selective for HER-2/neu would cross react with and be sequestered by, other members of the EGFR family. It particular, it is known that anti-tumor antibodies must accomplish several tasks to be effective. They must be delivered into the circulation that supplies the tumor and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. Also, the target cell must not have an alternate means of survival despite action at the proper site for the anti-tumor antibody. In addition, variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The antibody may be inactivated in vivo before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half life of the antibody. In addition, the antibody may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the antibody has no effect, circulation into the target area may be insufficient to carry the antibody and a large enough local concentration may not be established. This is clearly critical when considering the homology of HER-2/neu to the EGFR family. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill

in the art to predict that the broadly claimed method will function as claimed with a reasonable expectation of success.

Applicant's arguments drawn to the previous rejection of claims 19, 27-29 are relevant to the instant rejection.

Applicant argues that amendment of claim 19 satisfies the enablement rejection. The argument has been considered but has not been found persuasive because claim 19 was amended to recite that the antibody is "specific" for Her-2/neu protein, not "selective. In particular, Roitt et al, (Immunology, 1993, Mosby, St. Louis, p 6.4-6.5) teaches that when the determinants of antigen A are shared by another antigen, B, then antibodies that bind to those determinants in A will also react with B. This phenomenon is termed cross-reactivity (see Fig 6.8 on page 6.4 and p. 6.5, para 1), thus antibody that "binds specifically" to Her-2/neu will also bind specifically to other proteins of the EGFR family that share the same determinants.

8. It is noted that while claim 19 is enabling for therapy of androgen-dependent prostate cancer with anti-HER-2/neu antibody alone for the reasons set forth in the specification, pages 87-96, the claim reads on the treatment of all prostate cancers (including the claimed androgen-independent prostate cancer) with said antibody alone and the specification does not support the breadth of this claim. Thus, if Applicant were able to overcome the rejection set forth above claims 19 and claim 30 would still be rejected under 35 USC 112, first paragraph because the specification, while enabling for a method of treating androgen-independent prostate cancer in a subject in need of such treatment wherein said androgen-independent prostate cancer overexpresses HER-2/neu comprising administering to the subject therapeutically effective amounts of humanized monoclonal antibody

that binds the extracellular domain of the Her-2/neu protein in combination with paclitaxel, does not reasonably provide enablement for said method comprising treating said all prostate cancers with humanized monoclonal antibody that binds the extracellular domain of the Her-2/neu protein alone. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected to practice the invention commensurate in scope with these claims.

The claims are drawn to a method of treating prostate cancer/androgen-independent prostate cancer in a subject in need of such treatment wherein said androgen-independent prostate cancer overexpresses HER-2/neu comprising administering to the subject therapeutically effective amounts of humanized monoclonal antibody that binds the extracellular domain of the Her-2/neu protein. This means a treatment with Her-2/neu antibody alone. The specification teaches the immunohistochemically identified membrane overexpression of HER-2/neu in primary prostate cancer samples, see pages 87-96, and further teaches the treatment, in pre-clinical models, of cell-line derived androgen-independent sublines of CWR22 with the known, effective HER-2/neu antibody, HERCEPTIN. The specification teaches that no effect of HERCEPTIN on tumor growth was observed in any of the androgen independent tumors (p. 103, lines 16-17). When paclitaxel was given to animals with independent tumors, there was growth inhibition in each group. Paclitaxel and HERCEPTIN cotreatment led to greater growth inhibition than was seen in the agents individually (para bridging pages 103-104).

One cannot extrapolate the teaching of the specification to the scope of the claims because the specification clearly teaches that HERCEPTIN alone, the

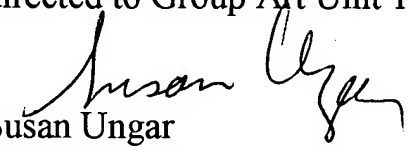
successful anti-HER-2/neu antibody cancer therapeutic, had no effect on tumor growth. Given the specification's clear demonstration of lack of effect of HERCEPTIN alone, the claimed invention is not enabled.

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.



Susan Ungar
Primary Patent Examiner
October 14, 2005